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EXAMINER	
JAGOE, DONNA A	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/802,000	THOMAS, THOMAS NADACKAL	
	Examiner	Art Unit	
	Donna Jagoe	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *6,8-16,18,19 and 21-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7,17 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments filed April 7, 2008 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1-34 are pending.

Claims 1-5, 7, 17 and 20 are rejected.

Claims 6, 8-16, 18, 19 and 21-34 are withdrawn from consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 and 7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of side effects of NSAIDS and providing tissue protection, it does not reasonably provide enablement for preventing side effects of NSAIDS. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). These include: nature of the invention, breadth of the claims, guidance of the

specification, the existence of working examples, and predictability of the prior art, state of the prior art and the amount of experimentation necessary. All of the **Wands factors** have been considered with regard to the instant claims, with the most relevant factors discussed below.

A. Breath of the Claims: The complex of nature of the claim is greatly exacerbated by breath of the claim. The claims encompass prevention of the side effects of anti-inflammatory drugs which have potentially many different presentations (Non-steroidal anti-inflammatory drugs (NSAIDs) are associated with a number of side effects. The frequency of side effects varies between the drugs. The most common side effects are nausea, vomiting, diarrhea, constipation, decreased appetite, rash, dizziness, headache, and drowsiness. NSAIDs may also cause fluid retention, leading to edema. The most serious side effects are kidney failure, liver failure, ulcers and prolonged bleeding after an injury or surgery. Steroidal anti-inflammatory drugs, such as cortisone has side effects such as problems with your vision, swelling, rapid weight gain, feeling short of breath, severe depression, unusual thoughts or behavior, seizure, bloody or tarry stools, coughing up blood, pancreatitis, low potassium (confusion, uneven heart rate, extreme thirst, increased urination, leg discomfort, muscle weakness or limp feeling) or dangerously high blood pressure (severe headache, blurred vision, buzzing in your ears, anxiety, confusion, chest pain, shortness of breath, uneven heartbeats, seizure). Less serious side effects may include insomnia, mood changes, acne, dry skin, thinning skin, bruising or discoloration,

slow wound healing, increased sweating, headache, dizziness, spinning sensation, nausea, stomach pain, bloating, or changes in the shape or location of body fat (especially in your arms, legs, face, neck, breasts, and waist).

Each of these defects may or may not be addressed by the administration of the claimed compounds.

B. Nature of the Invention: Claims 1 and 7 are drawn to a method of preventing, reducing and reversing the toxic effects of anti-inflammatory drugs and enhance their beneficial effects, comprising administering to a subject an effective amount of deprenyl or propargylamine compounds. The nature of the invention is

extremely complex in that it encompasses the actual prevention of an undisclosed side effect of an anti-inflammatory medication.

C. State of the Prior Art: While the state of the art is relatively high with regard to treatment of specific side effects, such as gastrointestinal distress, the state of the art with regard to **prevention** of all side effects of anti-inflammatory drugs is underdeveloped. In particular, there do not appear to be any examples or teachings in the prior art wherein a compound similar to the claimed compounds was administered to a subject to **prevent** all of the above possible side effects of anti-inflammatory drugs.

D. The Level of One of Ordinary Skill: The relative skill of those in the art is generally that of a physician.

E. Predictability of the Art: The lack of significant guidance from the specification or prior art with regard to the actual **prevention** of side effects of anti-inflammatory drugs with the claimed compounds makes practicing the claimed invention unpredictable.

F. Guidance of the Specification: The guidance given by the specification as to which medications are administered and which side effects are prevented is minimal.

G. Working Examples: All of the working examples provided by the specification are directed toward the inhibition of gastrointestinal side effects of NSAIDs.

H. The amount of Experimentation Necessary: In order to practice claimed invention, one of skilled in the art would have to first envision a combination of appropriate pharmaceutical carrier, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system for one of the claimed MAO A or MAO B inhibitors and an appropriate anti-inflammatory agent and test the combination in the model system to determine whether or not the combination is effective for **prevention** of any side effects, which is unclear because it is not disclosed which side effect one would look for, except for inhibition of gastrointestinal side effects from NSAIDs. If unsuccessful, which is likely, given the lack of significant guidance from the specification or prior art with regard to prevention of side effects from anti inflammatory agents, one of skill in the art would have to then either envision a modification of the regimen,

composition dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above, and test the system again. If again unsuccessful, which is likely given the lack of significant guidance from the specification of prior art regarding prevention of side effects with an anti inflammatory agent, the entire, unpredictable process would have to be repeated until successful. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to prevent the development of side effects of an anti inflammatory agent in a subject by administration of one of the claimed compositions.

Therefore, a method of **preventing** side effects from an anti inflammatory agent is not considered to be enabled by the instant specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 7, 17 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 1 and 20, the method wherein the anti-inflammatory drug and MAO inhibitor **can be** chemically linked, physically mixed or administered separately is indefinite because it is unclear whether it is linked by the recitation of the words "can be".

Regarding claim 4, the phrase "for example" (see line 7 of the claim) renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 1 recites the narrow recitation "administration of an effective amount of deprenyl or propargylamine compounds", and the claim also recites "(monoamine oxidase [MAO] inhibitors)" which is the broader statement of the range/limitation.

The term "natural anti-inflammatory agents" in claims 2 and 4 is a relative term which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a reasonable standard for ascertaining the requisite degree, and thus

one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Since no guidance is provided as to how "unnatural" a given value can be and still fall within the scope of the instantly claimed subject matter as circumscribed by the term "natural anti-inflammatory" the metes and bounds of the term are not clear, making it impossible to ascertain with reasonable precision when that term is infringed and when it is not.

Claim 17 recites the limitation "A method according to claim 6, wherein-the MAO inhibitor prevents or treats the toxic side effects of NSAIDS and provides tissue protection when administered as a separate compound or the MAO inhibitor is chemically linked to the NSAID". There is insufficient antecedent basis for this limitation in the claim because claim 6 is drawn to a composition; it is not drawn to a method.

Claim 20 is indefinite to the extent that it reads on the rejected base claim.

Regarding claim 20, the phrase "for example" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Regarding claim 20, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 20 is rejected as failing to define the invention in the manner required by 35 U.S.C. 112, second paragraph.

The claim(s) are narrative in form and replete with indefinite and functional or operational language. The structure which goes to make up the device must be clearly and positively specified. The structure must be organized and correlated in such a manner as to present a complete operative device. The claim(s) must be in one sentence form only. Note the format of the claims in the patent(s) cited.

Regarding claim 20, the phrase "a free amino group is introduced at the propyl carbon by arts known in the literature" renders the claim(s) indefinite because the claim(s) include(s) elements not actually disclosed (those encompassed by "known in the literature"), thereby rendering the scope of the claim(s) unascertainable.

Regarding claim 20, the phrase "and other NSAIDS to which a –COOH group can be attached" renders the claim(s) indefinite because the claim(s) include(s) elements not actually disclosed (those encompassed by "other NSAIDS to which a -COOH group can be attached"), thereby rendering the scope of the claim(s) unascertainable.

Regarding claim 20, the phrase "different MAO inhibitors and derivatives thereof can be attached to different NSAIDS by other methods known in the literature" renders the claim(s) indefinite because the claim(s) include(s) elements not actually disclosed (those encompassed by " different MAO inhibitors and derivatives thereof can be attached to different NSAIDS by other methods known in the literature "), thereby rendering the scope of the claim(s) unascertainable.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-5, 7, 17 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glavin et al. (cite No. 4 IDS dates 3/16/04) and Lianping et al (U).

Glavin et al. teach there is an association between the occurrence of duodenal ulcers and dopamine deficiency in disorders such as Parkinson's disease. In addition, disorders characterized by excess dopamine activity, such as schizophrenia are rarely associated with duodenal pathology. It was shown that pretreatment with a selective MAO_b inhibitor, L-deprenyl, prevented duodenal ulcers in rats when they were administered the agent 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). (see page 379)

It does not teach a method of preventing, reducing, and reversing the toxic effects of anti-inflammatory drugs comprising administration of an MAO inhibitor.

Lianping et al. teach MAO inhibitors reduced restraint stress-induced gastric ulceration by inhibition of gastrin release (page 61) resulting in a protection of the gastric mucosa (page 63, column 1).

It does not teach a method of preventing, reducing, and reversing the toxic effects of anti-inflammatory drugs comprising administration of an MAO inhibitor.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to employ MAO inhibitors to prevent the toxic effects of anti-inflammatory agents motivated by the teaching of Glavin et al. that L-deprenyl, prevented duodenal ulcers in rats when they were administered the agent 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), a dopamine depleting agent, known to cause gastric mucosal injury, thus demonstrating the protective utility of MAO inhibitors and by the teachings of Lianping et al. who demonstrates further inhibition of stress induced gastric ulceration by administration of MAO inhibitors to rats whereby release of gastrin is inhibited.

The protective gastrointestinal effect is disclosed in both references. It would have been obvious to employ the MAO inhibitors to provide a protective effect to the gastrointestinal mucosa when NSAIDs are administered.

One of ordinary skill in the art would have been capable of applying this known technique to a known method that was ready for improvement and the results would have been predictable to one of ordinary skill in the art.

Thus the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Accordingly, for the above reasons, the claims are deemed properly rejected and none are allowed.

Response to Arguments

Regarding the 35 U.S.C. § 112, first paragraph, Applicant contends that an invention does not need to be completely tested to satisfy the enablement requirement, the specification does not require working examples and does not need an example if the invention may be used without undue experimentation. Regarding this analysis, the examiner is in agreement. The specification does not require working examples, however, the features upon which applicant relies (i.e., gastrointestinal side effects) are not specifically recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The issue at hand is the unpredictability of preventing any side effect that would occur as a result of the administration of a NSAID or SAID.

Applicant states that "not every embodiment or procedure to practice the invention need to be disclosed for the invention to be enabled. In response, MPEP 2164.08(b) states that the standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art. Atlas Powder Co. v. E.I. du Pont de Nemours & Co., 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984) (prophetic examples do not make the disclosure nonenabling). However, claims reading on **significant numbers of inoperative embodiments** would render claims

non-enabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative. Atlas Powder Co. v. E.I. duPont de Nemours & Co., 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984); In re Cook, 439 F.2d 730, 735, 169 USPQ 298, 302 (CCPA 1971). In the instant case, the potentially inoperative embodiments include rash, dizziness, headache, drowsiness, fluid retention, leading to edema, kidney failure, liver failure, ulcers and prolonged bleeding after an injury or surgery, problems with vision, swelling, rapid weight gain, feeling short of breath, severe depression, unusual thoughts or behavior, seizure, bloody or tarry stools, coughing up blood, pancreatitis, low potassium, confusion, uneven heart rate, extreme thirst, increased urination, leg discomfort, muscle weakness or limp feeling) or dangerously high blood pressure, severe headache, blurred vision, buzzing in your ears, anxiety, confusion, chest pain, shortness of breath, uneven heartbeats, seizure, insomnia, mood changes, acne, dry skin, thinning skin, bruising or discoloration, slow wound healing, increased sweating, headache, dizziness, spinning sensation, changes in the shape or location of body fat Since the instant specification does not clearly identify the operative embodiments, the claims are not enabled. Applicant states that preventative and reductive treatments for anti-inflammatory drugs, such as synthetic prostaglandins, proton pump inhibitors and vitamin C have been tested for effectiveness in treating and preventing anti-inflammatory side effects. In response, these agents are tested in response to *gastrointestinal* side effects of anti-inflammatory drugs. The treatment of the side

effects recited above could not be prevented with reasonable assurity when using the recited method.

In response to applicant's argument that Lianping and Glavin is nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, the protective gastrointestinal effect is disclosed in both references. It would have been obvious to employ the MAO inhibitors to provide a protective effect to the gastrointestinal mucosa when NSAIDs are administered. One of ordinary skill in the art would have been capable of applying this known technique to a known method that was ready for improvement and the results would have been predictable to one of ordinary skill in the art. In response to applicant's argument that Liamping does not rely on dopamine functions to modulate the side effects of anti-inflammatory drugs but rather relies on the antioxidant, free radical scavenging properties of MAO inhibitors, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208

USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Friday from 8:00 A.M. - 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Donna Jagoe /D. J./
Examiner
Art Unit 1614

August 18, 2008

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614